Useng UnifiedModeling Language To Model The Immune System in Object Orientasi Perspective

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Using Unified Modeling Language to Model the Immune System in Object Oriented Perspective

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Abstract—**Artificial Immune System (AIS) has become known as an area of computer science and engineering that uses immune system metaphors solves problems with a novel solutions. The immune system has an interesting area for computer scientists with its uniqueness and fascinating computational system that has evolved to solve a unique problem. A deeper understanding of the immune system, in part through the use of modelling techniques, which will lead to the development of richer, more effective immune inspired engineered systems. It can suggest new solutions to computer science problems, or at least give us new ways of looking at these problems. This paper shows that bio-systems like immune system can be modelled using the object oriented perspective. We use Unified Modeling Language to represent the behavior of immune system and the interaction between immune system elements. The introduction motivates the need of immune system modeling at different levels of abstraction. Then the UML diagrams are used to illustrate the static and the dynamic behavior of immune system. There are an examples model for elementary clonal selection that involved B-cell, antibodies, and antigen correspondences. Since there are 14 (fourteen) diagrams of UML, this paper uses some of the diagrams. There are the use-case diagram to show functionality of immune system, activity diagrams to show the global abstractions of system and the class diagram to show the structure of immune system elements. At the conclusion, we can see that OO perspectives are promising the better understanding for complex bio-systems such as immune system. This is lead to get the better bio-inspired computation solutions to solve computer science problems.**

Keyword: Artificial Immune System, Immune System, Object Oriented, Unified Modeling Language.

I. INTRODUCTION

A. Background

Artificial Immune Systems (AIS) began in the mid 1980s, that uses the vetebrata immune system metaphors for the create new solutions to complex problems or at least gives new ways of looking at these problems. AIS are class of computationally intelligent systems which is a diverse area of research between immunology and engineering and becomes a bridge between them. Scope of AIS ranges from immune-inspired algorithms and engineering solutions in software and hardware, to the understanding of immunology through modeling and simulation of immune system concepts. The original research in AIS focus on applying immunological principles to computational problems in practical domains in a wide variety of domains, including machine learning, computer security, fault tolerance, bioinformatics, data mining, and optimization. As the field has matured, it has diversified such as formalizing the theoretical properties of earlier approaches, elaborating underlying relationships between applied computational models and those from theoretical immunology.

In recent years, the area of AIS has begun to return to immune system modeling, the immunology from which the initial inspiration came. Increasingly, theoretical insight into aspects of artificial and real immune systems has been sought through mathematical and computational modelling and analysis. This vigorous field of research investigates how immunology can assist our technology, and along the way is beginning to help biologists understand their unique problems.

To capture the complexity and richness that the immune system offers is a difficult part for AIS practitioners [1]. Many of them were failing. In order to remedy this, Stepney et., all. suggest a conceptual framework [2] for developing bio-inspired algorithms within a more principled framework that attempts to capture biological richness and complexity, but at the same time appreciate the need for engineered systems.

Recently, AIS towards paying more attention to taking time both to develop abstract computational models of the immune system and work closer with immunologists to better understand the biology behind the system. This would be fair to say that AIS is becoming a more inter-disciplinary topic where people are working more on the biological aspects and others on the more engineering aspects [2][3].

B. Problem Identification

One of the main problems involved in designing bio-inspired algorithms, is deciding which aspects of the

biology are necessary to generate the required behaviour, and which aspects are surplus to requirements.

Some of the properties of the immune system show the richness and complexity of the system. It might be of interest to a computer scientist to inspire the novel solutions of complex problems. There are some properties of the immune system: [4]

- The immune system is unique, it is different for each individual.
- The immune system has distributed detection with small and efficient detectors and are not subject to centralized control or coordination.
- The immune system is not requiring absolute detection of every pathogen, it can trade off resources used on protection for comprehensiveness of coverage.
- The immune system can detect and react to foreigns molecules and materials, that the body has never before encountered.
- The immune system can learn the structures of pathogens, and remember those structures, so that future responses to the pathogens can be much faster.

The immune system uses distributed detection to solve the problem of distinguishing between self and nonself, which are elements of the body, and foreign elements respectively. Actually, the success of the immune system is more dependent on its ability to distinguish between harmful nonself, and everything else.

Within the complexity and richness from the immune system, with the context of the conceptual framework, modelling plays an important role in the understanding of the computational aspects of the immune system. Andrews and Timmis [3], Bersini [6] makes the argument that the AIS practitioner should take more seriously the role of modelling in the understanding and development of immune inspired solutions, and adopt a more "artificial life" approach. [7].

The problem is how to model the immune system, represents simple form with its complexity without reduce the richness from it.

C. *Purpose*

With several techniques to model immune system and theis advantages and disadvantages, this papers purpose to model the immune system from different view with object oriented perspective. This approach should be lead to better understanding of the immune system at computational aspect, since object oriented perspectives is a natural point of view.

We will use Unified Modeling Language as a standard language for modelling object, with dynamic and static behavior.

D. *Methodology*

This paper is orginized with this methodology:

- Immune system as literatur study
- Object oriented perspective modelling
- Using UML to model immune system

II. IMMUNE SYSTEM AND HOW IT WORKS

A. *Overview of Immune System*

The immune system is a network of cells, tissues, and organs that work together to defend the body against attacks by "foreign" invaders.

Immune system involves two main objects:

- immune cells that defens, and
- pathogens that cause infection.

A pathogen is a microscopic organism that causes sickness. Viruses and bacteria are examples of pathogens. On the surfaces of bacteria and viruses, there are antigens. An antigen is a foreign substance that stimulates the immune system to response.

B. *Structure of Immune System*

The immune system consist of cells that work together with different proteins to seek out and destroy anything foreign or dangerous that enters our body [4]. We group immune cell onto three big categories, can be seen at table above:

Table 1 Immune System Elements

No	Immune Cell Categories	Description	Main Task
1	Complement System	Group of proteins (made up of about 25 proteins) that flow freely in the blood and can quickly reach the site of an invasion where they can react directly with tigens.	Work together to assist or to complement the action of antibodies in destroying bacteria.
2	Phagocytes (the granulocyte, the macrophage, and the dendritic cell)	This is a group of immune cells specialized in to seek out and ingest anything foreign or dangerous (bacteria,viruses), and dead or injured body cells.	The phagocytes attack any invaders in large numbers, and destroy them. The macrophages alerts the rest of the immune system of invaders.
3	Lymphocytes cells and B cells)	White blood cells produced in the bone marrow then migrate to lymph nodes, spleen, and thymus.	Seek and find an antigen (match their specific receptors). Coordinate immune responses by communicating with other, Produce antibodies, Directly attack antigen or destroy infected cells.

This table resumes the detail of object in lymphocytes cell, there are Receptor, Lymph vessel, T-Cell, MHC, and B-Cell [4].

Table 2 Lymphocytes cell and others

No	Immune Cell	Description	Main Task

	Categories		
1	Receptor	On the surface of each lymphatic cell are receptors that enable them to recognize foreign substances.	Match one specific type of antigen. (The lymphocyte cell has receptors that can only match one specific type of antigen).
2	The Lymphatic system/ lymph vessels	A transportation system - for transportation and storage of lymphocyte cells within the body.	Transportation and storage of lymphocyte cell within the body. Adds cells into the body and filters out dead cells and invading organisms such as bacteria.
3	T Helper Cells (Th Cell)	T Helper Cells are one of type of T-cell. White blood cells produced in the bone marrow then migrate to the thymus to mature.	Coordinate immune responses by communicating with other cells. Stimulate B cells to produce antibodies, Activate other T cells
4	T Killer Cells (Cytotoxic T Lymphocytes – CTLs).	T Killer Cells are one of type of T-cell. White blood cells produced in the bone marrow then migrate to the thymus to mature	Directly attack other cells carrying certain foreign or abnormal molecules on their surfaces.
5	Major Histocompatibility Complex, or MHC. MHC class I and MHC class II.	MHC molecules are proteins recognized by T cells when they distinguish between self and nonself. A self-MHC molecule provides a recognizable scaffolding to present a foreign antigen to the T cell.	In most cases, T cells only recognize an antigen if it is carried on the surface of a cell by one of the body's own major histocompatibility complex, or MHC molecules.
6	B Cells	Lymphocytes that are produced in the bone marrow and later move to the spleen.	Secreting antibodies, that ambush foreign antigens circulating in the bloodstream. Each B cell is programmed to make one specific antibody.
7	Cytokines	chemical messengers to communicate among cells of the immune system. secreted by immune cells and act on other cells	Messenger among cells to coordinate appropriate immune responses. Between macrophages and T-helper, and between T-helper and B-cells..

C. Immune System and How It Works

Immune system has several ways to protect our body:

- Creating a barrier that prevents bacteria and viruses from enteringbody.
- Detecting and eliminating viruses or bacteria before they have a chance to reproduce and proliferate), or eliminating them that have managed to reproduce in sufficient numbers to start causing problems.
- Finding cancerous (or other unwanted cells) and eliminating them

This is a multi-layered architecture, with defenses on many levels. First layer is the skin and physiological barier such as pH and temperature. If pathogens have broken the first layer, they are dealt with by the innate immune system and by the acquired immune response system.

- The innate immune system primarily consists of the phagocytes that are roaming and ingesting non-self molecules and materials then clearing the system of both debris and pathogens.
- The acquired immune involves a host of cells, chemicals and molecules and response adaptively depends on foreign types. [4].

Here is the description of the acquired immune response:

1. The immune response typically is activated when a pathogen enters the body. Macrophages detect pathogens, ingest them and broke down into fragments, and display the antigen fragment on their cell surfaces. This is called antigen-presenting cells, the macrophages with antigen fragments displayed on their surfaces. An antigent-presenting macrophage interacts with a T Helper Cell that recognizes the same antigen.
2. The macrophages release a chemical alarm signal called Interleukin-1, which stimulates the T Helper Cell to secrete Interleukin-2. Interleukin-2 causes the activation of T-Killer Cells (Cytotoxic T cell) and B cells.
3. The immune responses from this point follows two paths, one using Cytotoxic T cell and one using B-cells:
   a) Using Cytotoxic T cell:
      i) There are antigen presenting cells displayed on infected cell's surfaces. An infected cells can also digest some of the pathogens and display antigen fragments on their cell surfaces.
      ii) The body makes millions of different type of Cytotoxic T Cells (CTLs).
      iii) Each type is able to recognize a particular antigen. They are capable of recognizing the antigen displayed on the surfaces of infected cells
      iv) The CTLs bind to the infected cells and produce chemicals that kill the infected cell.
   b) Using B-cells:
      i) The body makes millions of different type of B cells and their spesific receptor. Each B-cell able to recognize a particular antigen.

ii) When B-cell recognize a particular antigen, B cells become activated (by T Helper Cells), they clone theirself into several B-cells with same receptor.

iii) B-cells differentiate into plasma cells that secretes antibodies flooding the bloodstream then can bind to the antigen involved in this infection.

iv) Antibodies bind to the antigens on the surfaces of the pathogens, marking them for ingestion by macrophages.

v) Some of the B cells become memory B cells that may live for long life times. These memory B cells make the secondary immune response to a future infection which is swifter and stronger.

III. USING UML TO MODEL IMMUNE SYSTEM

A. Modelling the Immune System

This section present an overview of some of the techniques that are common place in the immunological world [5]. There are a number of ways in which one can model the immune system, with each approach offering different perspectives to the modeller.

Approach	Advantages	Disadvantages
Agent Based Modelling [5][8]	possible to observe quite easily the dynamics of the agent population that arise as a result of the interactions between the agents.	Difficult to define the right level of abstraction for each agent in the model, as this will clearly affect how the simulation operates.
Mathematical models [5][8]	Conventional tools, can be understood to many people	Lack of representation in higher abstraction
OO ways [5][6][7]	Familiar to software developer, it can ease to build the tools	Need detail representations

B. Unified Modeling Language

UML is a standardised specification language that can be used for general purpose modelling allowing for the creation of an abstract model of the system under study. Contained within UML is a wide variety of notions and figures that allow for the construction of the model. [8]

UML model has a set of diagrams to represent tje system. A diagram is a partial graphic representation of a system's model. The model also contains documentation that drives the model elements and diagrams. UML diagrams represent two different views of a system model:

- Static (or structural) view: emphasizes the static structure of the system using objects, attributes, operations and relationships. The structural view includes class diagrams and composite structure diagrams. There are seven diagram types represent structural information.
- Dynamic (or behavioral) view: emphasizes the dynamic behavior of the system by showing collaborations among objects and changes to the internal states of objects. This view includes sequence diagrams, activity diagrams and state machine diagrams. There are seven represent general types of behavior, including four that represent different aspects of interactions.

UML diagrams can be categorized hierarchically as shown in the following class diagram:

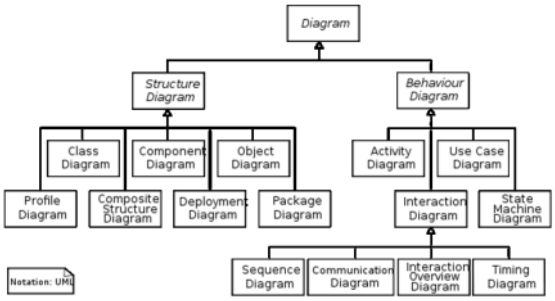

Figure 1 UML Diagrams [8]

C. UML Static View of Immune System

From static or structural viw, immune system as shown in the following class diagram:

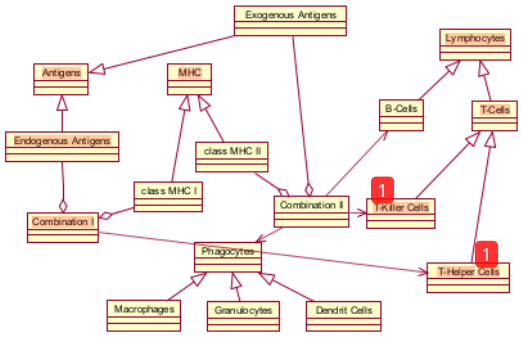

Figure 2 Static View of Immune System

There are Antigen, MHC, Lymphocytes, Phagocytes with their inherites.

D. UML behavioral view of Immune System

In OO perspective, we can see immune system as "business use-case" and the pathogens are a "business actor". If we see the immune system as a collection of functions, it can be represented using use-case diagrams. Each use-case represents their functionality of immune system. There are use-case of antigen presenting process (with exogenous antigen and endogenous antigen), Recognition (by B-cells and by T-cells), Destruction (by Phagocytes or Macrophages)

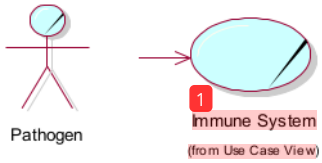

Figure 3 Immune System as "Business" Modelling

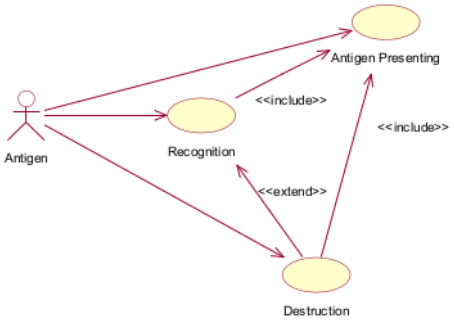

Figure 4 Functionalities of Immune System using Use-case Diagrams

Each use case will need detail activities that can be shown using Activity Diagrams.

1) Exogenous Antigen precenting process

If the antigen originates outside the cell, some phagocytes such as macrogphages ingest foreign particles such as viruses and bacteria. The foreign particles are broken down into fragments and combine with MHC class II. Then it's transported to the plasma membrane. The displayed MHC classII /antigen complex can stimulate other system cells to respon to the antigen. This process can we see in the following activity diagram:

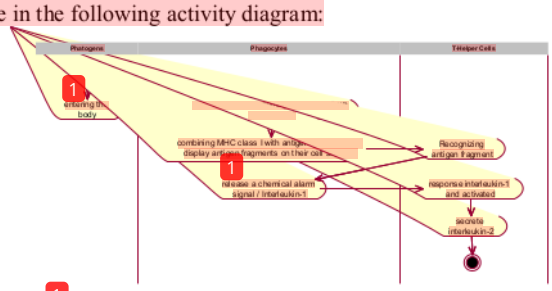

Figure 5 Exogenous Antigen Presenting Activity Diagram

2) Endogenous Antigen presenting process (from infected cells)

This is a process to display antigen-fragment on phagocytes's survaces. This process depends on whether the antigen originate, within or outside the cell. If the antigens are within the cell, the antigens are combined with class I MHC molecules. Foreign antigens presented on class I MHC molecules stimulate T cells. This process can we see in the following activity diagram:

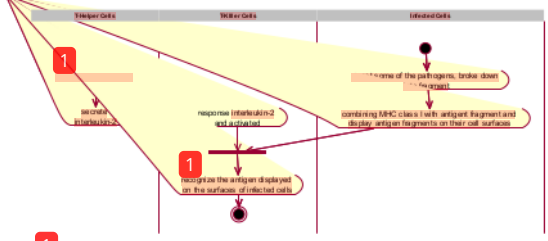

Figure 6 Endogenous Antigen Presenting Activity Diagram

3) Recognition (B-cells)

Recognition process by B-cell is the most important event from immune system process. B-cells is produced in the bone marrow and transported to spleen to make their diversity depend on their receptors. This B-cells should be activated before they release antibodies. This event needs T-Helper Cells to stimulate B-cells activation process. We use activity digrams to show that process:

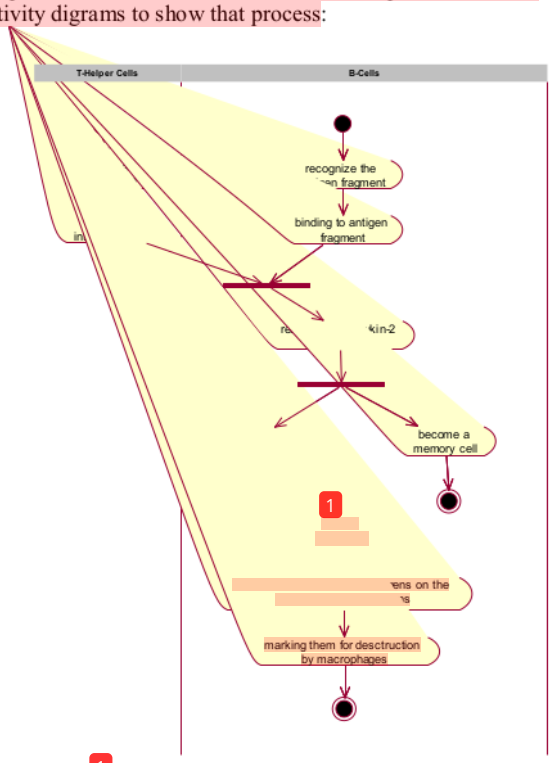

Figure 7 B-cells Recognition Activity Diagram

4) Desctruction by Phagocytes (Macrophages)

Antibody from B-cells will mark the antigens and then let another cells (macrophages) to destruct them.

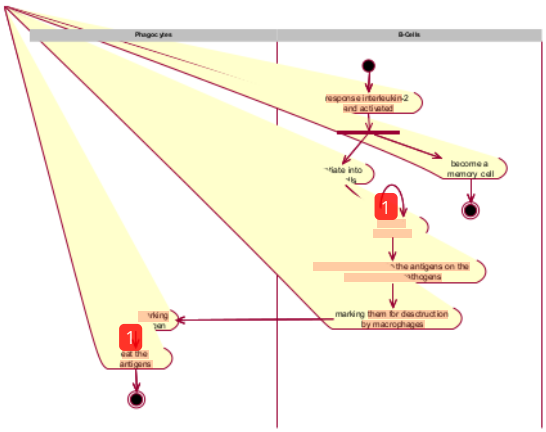

Figure 8 Destruction by Phagocytes

5) Recognition and Desctruction by T-cells

Different from B-cells, T-cells can destruct foreigns by themselves. They are T-killer cells or CTLs. This T-killer cells need to be activated by T-helper cells. We can see the process using this activity diagram as shown below:

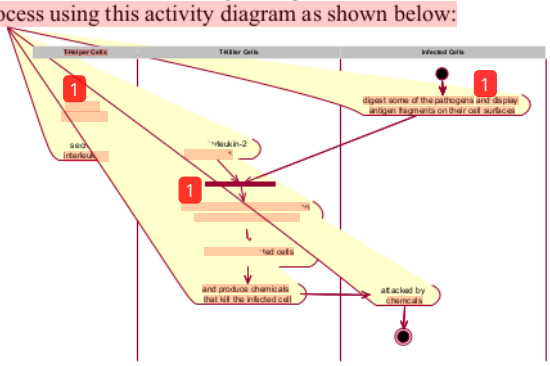

Figure 9 Recognition and Destruction by T-Killer Cells

IV. Further About B-cells Recognition

B-cells, T-helper cells, and T-killer cells will cooperate to recognize antigens by binding to them. Antigens are detected when a molecular bond is established between lymphocyte receptors and the antigens at their partscalled epitopes. A single lymphocyte can only bind to structurally related epitopes and it uses an approximate binding.

The number of receptors that bind to antigens will determine the affinity that the lymphocyte has for a given antigens. These Lymphocytes can only be activated by an antigen if the lymphocyte's affinity for the antigen exceeds a certain affinity threshold.

When a B-cell is activated, it differentiate into plasmacells and release antibodies. The B-cell also clones itself with the same receptor on their surfaces. According to genetic principle. The copies producted by cloning process. Cloning is need to subject to somatic hypermutation which can result in daughter cells that have somewhat different receptors from the parent. There are cloning process and somatic hypermutation in B-cells's life cycle.

V. Conclusion

Immune system can be modelled using OO perspectives. It promises the better understanding for complex bio-systems such as immune system. Especially for sofware engineer who will create computational solution to solve computer science problems. This paper only using three main UML diagrams, there are some diagrams will helpfull to represent the detail about immune system, such as B-cells recognition with their clonning process and somatic hypermutation.

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